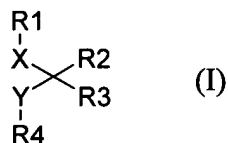


In the Claims:

Replace claims 2-8, 18, 28, 33, 41 and 42 with the amended versions below. Cancel claim 1. A complete list of the claims, whether amended herein or not, is presented below.

1. (canceled)

B4 2. (Currently amended) ~~The pharmaceutical~~ A formulation according to ~~claim 1~~ comprising:
(i) an inhibitor of carboxypeptidase U or a pharmaceutically acceptable salt thereof; and
(ii) a thrombin inhibitor or a derivative thereof,
in admixture with a pharmaceutically acceptable adjuvant,
diluent, or carrier, wherein the inhibitor of carboxypeptidase U is a compound of ~~general~~ formula I



or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,
wherein:

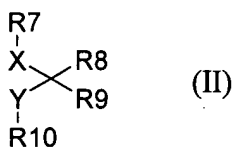
R₁ is selected from the group consisting of:

C₁-C₆ alkyl, substituted with one or more basic groups;
cycloalkyl, substituted with one or more basic groups;
heterocyclyl, comprising at least one nitrogen atom;
heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups;
and

aryl, substituted with one or more basic groups;

By
Am
R₂ is selected from the group consisting of H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl, aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, ~~oxo~~, nitro, thiol, a Z₂N-CO-O- group, a ZO-CO-NZ- group, and a Z₂N-CO-NZ- group;
R₃ is selected from the group consisting of COOR₅, SO(OR₅), SO₃R₅, P=O(OR₅)₂, B(OR₅)₂, P=OR₅(OR₅), tetrazole, and a carboxylic acid isostere;
R₄ is SH, S-CO-C₁-C₆ alkyl, or S-CO-aryl;
R₅ is H, C₁-C₆ alkyl, or aryl;
R₆ is H or C₁-C₆ alkyl;
X is selected from the group consisting of O, S, SO, SO₂, C(Z)₂, N(Z), NR₆SO₂, SO₂NR₆, NR₆CO, and CONR₆;
Y is C(Z)₂; and
Z is independently selected from the group consisting of H, C₁-C₆ alkyl, aryl, cycloalkyl and heterocyclyl.

3. (Currently amended) ~~The pharmaceutical~~ A formulation ~~according to claim 1,~~ comprising:
(i) an inhibitor of carboxypeptidase U or a pharmaceutically acceptable salt thereof; and
(ii) a thrombin inhibitor or a derivative thereof,
in admixture with a pharmaceutically acceptable adjuvant,
diluent, or carrier, wherein the inhibitor of carboxypeptidase U is a compound of ~~general~~ formula II,



or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein:

R₇ is selected from the group consisting of:

C₁-C₆ alkyl, substituted with one or more basic groups;
cycloalkyl, substituted with one or more basic groups;
heterocyclyl, comprising at least one nitrogen atom;
heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups; and
aryl, substituted with one or more basic groups;

R₈ is selected from the group consisting of H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl, aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, ~~oxo~~, nitro, thiol, Z₂N-CO-O-, ZO-CO-NZ-, and Z₂N-CO-NZ-;

R₉ is selected from the group consisting of COOR₁₁, SO(OR₁₁), SO₃R₁₁, P=O(OR₁₁)₂, B(OR₁₁)₂, P=OR₁₁(OR₁₁), tetrazole, and a carboxylic acid isostere;

R₁₀ is a $\text{P}(\text{O})(\text{O}-\text{R}_{11})(\text{R}_{12})$ -group, a $\text{C}(=\text{O})\text{N}(\text{R}_{13})\text{OH}$ -group, or a $\text{C}(=\text{O})\text{O}-\text{R}_{11}$ -group;

R₁₁ is H, C₁-C₆ alkyl, or aryl;

R₁₂ is C₁-C₆ alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted

H₂N-C(Z)-CONH-C(Z)- or H₂N-C(Z)- group;

R₁₃ is H or C₁-C₆ alkyl;

X is selected from the group consisting of O, S, SO, SO₂, C(Z)₂, N(Z), NR₁₃SO₂, SO₂NR₁₃, NR₁₃CO, and CONR₁₃;

Y is selected from the group consisting of O, N(Z), S, C(Z)₂, and a single bond; and

B11
Conclude
Z is independently selected from the group consisting of H, C₁-C₆ alkyl, aryl, cycloalkyl, and heterocyclyl, with the proviso that when X is O, S, SO, SO₂, N(Z), NR₇SO₂, SO₂NR₇, or NR₇CO, then Y is C(Z)₂ or a single bond.

B12
4. (Currently amended) The ~~pharmaceutical~~ formulation according to ~~any previous claim 2 or 3~~, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.

5. (Currently amended) The ~~pharmaceutical~~ formulation according to claim 4, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.

6. (Currently amended) The ~~pharmaceutical~~ formulation according to claim 5, wherein the low molecular weight thrombin inhibitor is HOOC-CH₂-(R)Cgl-Aze-Pab-H or a prodrug thereof.

7. (Currently amended) The ~~pharmaceutical~~ formulation according to claim 6, wherein the prodrug is EtOOC-CH₂-(R)Cgl-Aze-Pab-OH.

B13
8. (Currently amended) The ~~pharmaceutical~~ formulation according to ~~any one of claims 1-3~~ claim 2 or 3, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1000:1 to about 1:1000.

9. (Previously amended) A kit of parts comprising:
(i) a vessel comprising an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof;

(ii) a vessel comprising a thrombin inhibitor, or a derivative thereof; and
(iii) instructions for the sequential, separate or simultaneous administration of the inhibitors (i) and (ii) to a patient in need thereof.

10. (Previously amended) A kit of parts comprising:

(i) a vessel comprising an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof;
(ii) a vessel comprising a thrombin inhibitor, or a derivative thereof; and
(iii) instructions for the sequential, separate, or simultaneous administration of the inhibitors (i) and (ii) to a patient in need thereof,
wherein the inhibitor of carboxypeptidase U is a compound according to claim 2 or 3.

11. (Previously amended) The kit of parts according to claim 9, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.

12. (Original) The kit of parts according to claim 11, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.

13. (Original) The kit of parts according to claim 12, wherein the low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.

14. (Original) The kit of parts according to claim 13, wherein the prodrug is EtOOC-CH₂-(R)Cgl-Aze-Pab-OH.

15. (Previously amended) The kit of parts according to claim 9, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1000:1 to about 1:1000.

16. (Previously amended) A kit of parts comprising:

(i) a pharmaceutical formulation comprising an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier; and

(ii) a pharmaceutical formulation comprising a thrombin inhibitor, or a derivative thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier, wherein inhibitors (i) and (ii) are each formulated for administration in conjunction with the other.

17. (Previously amended) The kit of parts according to claim 16, wherein inhibitors (i) and (ii) are formulated for sequential, separate or simultaneous administration.

B14 18. (Currently amended) A kit of parts comprising:

(i) a ~~pharmaceutical~~ formulation comprising an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier; and

(ii) a ~~pharmaceutical~~ formulation comprising a thrombin inhibitor, or a derivative thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier,

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include*

wherein inhibitors (i) and (ii) are each formulated for administration in conjunction with the other, and wherein the inhibitor of carboxypeptidase U is a compound according to claim 2 or 3.

19. (Previously amended) The kit of parts according to claim 16 or 17, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.

20. (Original) The kit of parts according to claim 19, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.

21. (Original) The kit of parts according to claim 20, wherein the low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.

22. (Original) The kit of parts according to claim 21, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.

23. (Previously amended) The kit of parts according to claim 16, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1000:1 to about 1:1000.

25. (Previously amended) A method for the treatment of a patient suffering from, or susceptible to, a condition in which inhibition of thrombin and/or inhibition of carboxypeptidase U are required or desired, which method comprises administering to the patient a therapeutically effective total amount of:

- (i) an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and
- (ii) a thrombin inhibitor, or a derivative thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier.

26. (Previously amended) The method according to claim 25, wherein the administration of inhibitors (i) and (ii) is sequential, separate or simultaneous.

27. (Previously amended) A method for the treatment of a patient suffering from, or susceptible to, a condition in which inhibition of thrombin and/or carboxypeptidase U are required or desired, which method comprises administering to the patient a therapeutically effective total amount of:

- (i) an inhibitor of carboxypeptidase U, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier; and
- (ii) a thrombin inhibitor, or a derivative thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier,
- wherein the inhibitor of carboxypeptidase U is a compound according to claim 2 or 3.

B15 28. (Currently amended) The method according to ~~any one of~~ claims 25 or 26, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.

29. (Previously amended) The method according to ~~any one of~~ claims 28, wherein the low molecular weight thrombin inhibitor

is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.

30. (Previously amended) The method according to claim 29, wherein the low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.

31. (Original) The method according to claim 30, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.

32. (Previously amended) The method according to claim 25 or 26, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1000:1 to about 1:1000.

B16 33. (Currently amended) A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of thrombin and/or inhibition of carboxypeptidase U are required or desired, which method comprises administering to the patient a formulation according ~~any one of claims 1 to 3~~ to claim 2 or 3.

B17 41. (Currently amended) The ~~pharmaceutical~~ formulation according to ~~any one of claims 2 or 3~~, wherein the basic group is selected from the group consisting of amino, amidino, and guanidino.

42. (Currently amended) The ~~pharmaceutical~~ formulation according to ~~any one of claims 1 to 3~~ claim 2 or 3, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.

43. (Previously added) The kit of parts according to claim 10, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.
44. (Previously added) The kit of parts according to claim 43, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.
45. (Previously added) The kit of parts according to claim 44, wherein the new low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.
46. (Previously added) The kit of parts according to claim 45, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.
47. (Previously added) The kit of parts according to claim 9, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range from about 50:1 to 1:50.
48. (Previously added) The kit of parts according to claim 10, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range from about 1,000:1 to about 1:1,000.
49. (Previously added) The kit of parts according to claim 10, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range from about 50:1 to 1:50.

50. (Previously added) The kit of parts according to claim 18, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.
51. (Previously added) The kit of parts according to claim 50, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.
52. (Previously added) The kit of parts according to claim 51, wherein the low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.
53. (Previously added) The kit of parts according to claim 52, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.
54. (Previously added) The kit of parts according to claim 16, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.
55. (Previously added) The kit of parts according to claim 18, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1,000:1 to about 1:1,000.
56. (Previously added) The kit of parts according to claim 18, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.

57. (Previously added) The method according to claim 27, wherein the thrombin inhibitor is a low molecular weight thrombin inhibitor.
58. (Previously added) The method according to claim 57, wherein the low molecular weight thrombin inhibitor is a peptide-based, amino acid-based, and/or peptide analogue-based, thrombin inhibitor with one to four peptide linkages.
59. (Previously added) The method according to claim 58, wherein the low molecular weight thrombin inhibitor is $\text{HOOC-CH}_2\text{-(R)Cgl-Aze-Pab-H}$ or a prodrug thereof.
60. (Previously added) The method according to claim 59, wherein the prodrug is $\text{EtOOC-CH}_2\text{-(R)Cgl-Aze-Pab-OH}$.
61. (Previously added) The method according to claim 25, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.
62. (Previously added) The method according to claim 27, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 1,000:1 to about 1:1,000.
63. (Previously added) The method according to claim 27, wherein the molar ratio between the inhibitor of carboxypeptidase U and the thrombin inhibitor lies in the range of from about 50:1 to about 1:50.